

REMARKS

The present application is directed to pharmaceutical compositions containing combinations of an antibody and antibody fragment, combinations of antibody fragments, and methods of treatment using the compositions for various conditions, particularly conditions caused by toxins such as botulism.

Claims 1, 7-9, 11-18, and 23-24 are currently pending in the application. Claims 19 and 21 were previously withdrawn, and Claims 20 and 22 were previously cancelled. By this amendment, Claims 2-6, and 10 have been cancelled. Claim 1 is currently amended. No new matter has been added.

Advisory Action

In the Advisory Action mailed March 9, 2009, the Examiner stated that the amendments submitted in the Response filed February 16, 2009, reciting that the small binding fragment binds the “target toxin”, would require a new search and consideration. The Examiner also indicated that the amendments submitted in the Response filed February 16, 2009 will not be entered.

Applicants have amended Claim 1 to specify that the first specific binding agent is an F(ab')₂ or F(ab)₂ fragment of an antibody and the second specific binding agent is an Fab or Fab' fragment of an antibody, a single chain (sc) antibody, or FV, VH, or VK fragments. No new matter has been added by these amendments.

Rejection under 35 U.S.C. §102(b)

In the Office Action mailed December 15, 2008, the Examiner maintained the rejection of Claims 1-18 under 35 U.S.C. §102(b) as anticipated by, or in the alternative, under 35 U.S.C. §103(a) as obvious over Habermann *et al.* (*Med. Microbiol. Immunol.* Vol. 161, pp. 203-210, 1975; hereinafter “Habermann”). Applicants respectfully traverse the rejections.

Habermann describes an antitoxin containing *whole, intact* antibodies against botulinum toxins A, B, and E.

Applicants respectfully submit that Habermann fails to teach a composition containing the combination of a first binding agent, which is a fragment of an antibody, and a second binding agent, which is a small binding fragment of an antibody. In addition, Habermann fails to teach a composition having different types of binding agents that bind to the same toxin as claimed in the present application. One of skill in the art would understand that the term “binding agent” as used in Claim 1 does not mean an entire antibody. Furthermore, the terms are also clearly defined in the specification. In paragraph [0015] of the published application, the term for the first “binding fragment” is defined as “an antibody fragment that....will comprise the entire variable domain, as well as some of a constant region (Fc).” In particular, these antibody fragments are F(ab')₂ or F(ab)₂ fragments. In paragraph [0017] of the published application, the term “small binding fragment” is defined as “an antibody fragment which lacks a significant element of the antibody from which it is derived...In particular, small antigen binding fragments include Fab or Fab' fragments, as well as single chain (sc) antibodies, FV, VH, or VK fragments.” Consequently, despite the use of the term “comprising”, the claims clearly require that the composition contain a first binding agent *and* a second binding agent, wherein the second binding agent is *not* an entire antibody.

As noted earlier, Habermann fails to disclose a composition containing two different binding agents. Consequently, Habermann fails to disclose each and every element of, and therefore fails to anticipate, Claims 1, 7-9 and 11-18. Claims 2-6, and 10 have been cancelled. For at least the foregoing reasons, applicants respectfully assert that the rejection under 35 U.S.C. §102(b) has been overcome and request its withdrawal.

Alternative rejection under 35 U.S.C. §103(a)

With regard to the alternative rejection, under 35 U.S.C. §103(a), applicants submit that Claims 1, 7-9 and 11-18 are not obvious because Habermann fails to teach,

suggest or imply a composition containing fragments of an antibody. Habermann discloses a composition containing only *intact* antibodies as produced naturally. Furthermore there is no teaching, suggestion, or implication by Habermann to provide a composition containing *two different* binding agents (one of which is a small antibody fragment) that bind to the *same* toxin. Nothing in Habermann indicates that using antibody fragments in a composition would produce the superior results achieved by the claimed composition.

In addition, as noted in the specification, the claimed composition has many advantages and achieves unexpectedly good benefits over the compositions described in the art, such as Habermann. First, according to paragraph [0004] of the published application, using antibody fragments instead of whole antibodies has “the advantage of producing fewer side effects in the patients, and thus an improvement in safety.” Second, paragraph [0007] of the published application states that “[c]ompositions of the invention have been found [to] provide rapid and sustained antitoxin activity” which may be due in part to the “mutually complementary properties of the first and second specific binding agents to provide sustained antitoxin capability.” Habermann fails to teach this complementary combination, and specifically fails to teach the use of the second specific binding agent. The second specific binding agent, as discussed above, is a small binding fragment of an antibody, and “appears to provide an antitoxin capability that penetrates rapidly into the extravascular space to provide rapid protection” (paragraph [0008] of the specification).

For at least these reasons, applicants respectfully assert that the alternative rejection under 35 U.S.C. §103(a) has been overcome and request its withdrawal.

CONCLUSION

This response fully addresses the rejections in the Office Action mailed December 15, 2008. In light of the above remarks, applicants respectfully assert that the application is now in condition for allowance. Such action is respectfully requested.

If the Examiner believes any informalities remain in the application that may be corrected by Examiner's Amendment, or if there are any other issues that can be resolved by telephone interview, a telephone call to the undersigned attorney at (404) 815-6591 is respectfully solicited.

No additional fees are believed due; however the Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account number 11-0855.

Respectfully submitted,

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